



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/570,122

02/28/2006

Christine Power

ARS.122

7430

23557 7590 06/15/2011  
SALIWANCHIK, LLOYD & EISENSCHENK  
A PROFESSIONAL ASSOCIATION  
PO Box 142950  
GAINESVILLE, FL 32614

EXAMINER

DEBERRY, REGINA M

ART UNIT

PAPER NUMBER

1647

NOTIFICATION DATE

DELIVERY MODE

06/15/2011

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slepatents.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/570,122	<b>Applicant(s)</b> POWER ET AL.	
	<b>Examiner</b> REGINA M. DEBERRY	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 14 April 2011.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 46-50,55 and 57-86 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 46-50,55 and 57-86 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

The finality of the rejection of the last Office Action (14 January 2011) is withdrawn in view of the rejection set forth below. Please see the Matter of Record section for a summary of the prosecution history and reasons why the prior art of record is not applicable.

Applicant's Request for Reconsideration and Arguments after Final Rejection have been entered (14 April 2011).

#### **Status of Application, Amendments and/or Claims**

Claims 1-45, 51-54, 56, are canceled. Claims 46-50, 55, 57-86 are pending and under examination.

#### **Withdrawn Objections And/Or Rejections**

The rejection to claims 46-50, 55, 57-86 under 35 U.S.C. 112, first paragraph, scope of enablement, as set forth at pages 2-7 of the previous Office Action (14 January 2011), is *withdrawn* in view of the new rejection below.

#### **Claim Rejections - 35 USC § 112, First Paragraph, Enablement**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46-50, 55, 57-86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains

Art Unit: 1647

subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The basis for this rejection is set forth at pages 4-7 of the previous Office Action (02 September 2008). The instant rejection is being reinstated for the following reasons.

The specification states that the present invention is in the field of fibrotic diseases/connective tissue disorders and the use of INSP035 for the treatment and/or prevention of fibrotic diseases. The specification teaches the full length cDNA of human INSP035 as SEQ ID NO:1 and the corresponding amino acid sequence as SEQ ID NO:2 (page 9, lines 23-26). The sequence listing teaches SEQ ID NO:2 as having 163 amino acids. The specification teaches the cDNA of human INSP035 starting at the 2nd methionine (called INSP035 medium form) from INSP035 has been cloned. The cDNA is SEQ ID NO:4 and the corresponding amino acid sequence is SEQ ID NO:5 (page 9, lines 26-29). The sequence listing teaches SEQ ID NO:5 as having 88 amino acid residues. The specification teaches that a modified INSP035 medium form with an isoleucine substitution at position 1 has been generated as SEQ ID NO:7 (page 9, lines 29-31). The sequence listing teaches SEQ ID NO:7 as having 88 amino acid residues.

The specification states that the invention is based on the finding that INSP035 is a potent inhibitor of TRAIL in an *in vitro* assay designed to select anti-apoptotic molecules in fibroblasts with osteoprotegerin (OPG) as control. The

Art Unit: 1647

specification states that like OPG, INSP035 is able to counteract the apoptotic effect of soluble human recombinant TRAIL on fibroblasts, thereby consistently reducing fibroblasts' apoptosis (page 7, lines 1-6). The specification states that administered OPG resulted in significant amelioration of fibrosis in an established animal model of lung fibrosis. The specification states that on the basis that OPG and INSP035 share common functionalities and on the findings that TRAIL stimulates collagen production, INSP035 is suggested to be useful in the treatment of fibrosis (page 8, lines 9-18).

The instant specification cites Taimr et al. (Hepatology, Vol. 37, No. 1, pages 87-95; 2003). The Examiner notes that this particular reference, while cited in the instant specification (page 6, lines 23-28), is not listed on any of the submitted IDS. It is made of record herein. Taimr et al. teach that extensive liver fibrosis, which results from the deposition and accumulation of type I collagen within the liver parenchyma, results in fibrosis. Taimr et al. state that understanding the mechanisms of liver fibrosis is essential to defining anti-fibrotic therapies (page 87, 1st paragraph). Taimr et al. teach that activated hepatic stellate cells (HSCs) have been established as the source of type I and III collagen in the liver. Activated stellate cells secrete type I collagen, the principal matrix protein responsible for the development of liver fibrosis and cirrhosis. Taimr et al. teach that because activated stellate cells are responsible for the exuberant and unbalanced wound healing response in cirrhosis, *their selective removal would be a potential mechanism to attenuate liver fibrosis* (page 87). *Taimr et al. teach that if TRAIL can induce selective apoptosis of activated*

Art Unit: 1647

*stellate cells, it would become a candidate anti-fibrotic agent.* Taimr et al. teach that the present study was to examine the relationship of stellate cells to TRAIL receptors and susceptibility of stellate cells to TRAIL mediated apoptosis (page 88). *Taimr et al. teach that their data suggests that TRAIL agonists could be used to reduce the number of activated stellate cells as a therapeutic approach to reduce fibrosis* (page 94, last paragraph).

Example 2 demonstrates that SEQ ID NO:2 (SEQ ID NO:5 and SEQ ID NO:7) inhibit the TRAIL protein in an in vitro assay. Example 5 is a prophetic teaching suggesting administered SEQ ID NO:2 will protect against lung fibrosis in mice.

The specification teaches ***that INSP035 is able to counteract the apoptotic effect of soluble human recombinant TRAIL on fibroblasts, thereby consistently reducing fibroblasts' apoptosis.*** However, Taimr et al. ***teaches the opposite biological affect; that if TRAIL can induce selective apoptosis of activated stellate cells, it would become a candidate anti-fibrotic agent.*** Thus, the instant specification teaches INSP035 as an antagonist of TRAIL, inhibiting TRAIL induced apoptosis to treat fibrosis. ***Conversely,*** Taimr et al. teach that TRAIL agonists would useful in treating fibrosis. The prophetic teaching in Example 5 discloses a model, however based on the teachings of Taimr et al. and the lack of working examples actually demonstrating administered INSP035 can treat liver or lung fibrosis in vivo, it is highly unpredictable what effect SEQ ID NO: 2, 5, and 7 would have when administered to a patient. The specification need not contain working examples if

Art Unit: 1647

the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. However, lack of working examples, is a factor to be considered, especially in cases involving unpredictable and undeveloped art. Such is the instant case. Based on the reasons above, it could not be predicted that the cell culture data presented in the instant specification would be in any way correlative with therapeutic agents for *in vivo* treatment of fibrotic diseases.

Lastly, the specification fails to teach how to treat a fibrotic disease *in vivo* using fragments and/or mutants of full length INSP035 (SEQ ID NO:2). SEQ ID NO:5 and SEQ ID NO:7 comprise 1/2 the amount of amino acid residues of SEQ ID NO:2. Further, SEQ ID NO:7 comprises a mutation. The disclosure provides no guidance as to which regions of the INSP035 protein would be tolerant of modification and which would not, and it provides no working example of any variant sequence (an actual *in vivo* treatment employing SEQ ID NO:5 and SEQ ID NO:7). The specification fails to teach the structural features that are required in order to provide the biological activity of inhibiting fibrosis. It is extremely complex to predict protein structure from sequence data and in turn utilizing calculated structural determinations to ascertain functional aspects of the protein. For example, the specification states that INSP035 was identified as a leptin (page 5, lines 10-21), but Figure 2 demonstrates that leptin did not affect TRAIL-mediated apoptosis, like INSP035 in the *in vitro* assay. Thus, it is in no way predictable that mutations, deletions, etc. in the disclosed sequence would afford a protein having activity comparable to the one disclosed.

Due to the large quantity of experimentation necessary to discern the structural features that are required in fragments and mutants of full length INSP035 (i.e. SEQ ID NO:5 and SEQ ID NO:7) to provide the claimed biological activity of inhibiting fibrosis in vivo, the inherent unpredictability in the field and the lack of guidance in the specification regarding a correlation between the presented in vitro data and the efficacy of administered INSP035 for treating liver or lung fibrosis in vivo, the lack of direction/guidance presented in the specification regarding same and the structural features required to provide the claimed activity, the absence of working examples directed to same, the complex nature of the invention and the state of the art which teaches the opposite biological effect of TRAIL that is needed to treat fibrosis, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

The scientific reasoning and evidence as a whole indicates that the rejection from 08 September 2008 should be reapplied.

#### **MATTER OF RECORD**

The Examiner stated (previous Office Action 2/24/09; pages 3-4) that claims 46-50, 55, 57-60 were rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al. (WO 02/074961 A1). The Examiner stated that Tang et al. teach a polypeptide (SEQ ID NO:913) that is 100% identical to instant SEQ ID NO:2 (See APPENDIX A). The Examiner stated that Tang et al. teach that a composition of the present invention is useful for treatment of lung or liver fibrosis (page 55, lines 24-26).



Art Unit: 1647

**APPENDIX A**

GenCore version 6.3

Copyright (c) 1993 - 2011 Bioceleration Ltd.

OM protein - protein search, using sw model

Run on: January 7, 2011, 10:46:43 ; Search time 34 Seconds  
(without alignments)  
5928.367 Million cell updates/sec

Title: US-10-570-122A-2  
Perfect score: 836  
Sequence: 1 MSLGLLKFQAVGEEDEDEE.....LLRHLGLTRMNISARRFTLC 163

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 6395994 seqs, 1224146475 residues

Total number of hits satisfying chosen parameters: 6395994

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : A\_Geneseq\_201023:\*  
1: geneseqp1:\*  
2: geneseqp2:\*  
3: geneseqp3:\*

## SUMMARIES

Result No.	Score	Query Match	Length	DB	ID	Description
1	836	100.0	163	1	ABU00294	Abu00294 Human nov

## ALIGNMENTS

## RESULT 1

ABU00294

ID ABU00294 standard; protein; 163 AA.

XX

AC ABU00294;

XX

DT 15-JUN-2007 (revised)

DT 17-JAN-2003 (first entry)

XX

DE Human novel polypeptide #387.

XX

KW Human; genetic disorder; gene mapping; medical imaging; cancer;  
KW neurodegenerative disorder; lymphoid cell disorder; osteoporosis;  
KW Parkinson's disease; Alzheimer's disease; bone degenerative disorder;  
KW osteoarthritis; periodontal disease; liver fibrosis; viral infection;  
KW fungal infection; bacterial infection; autoimmune disease; diabetes;  
KW atopic dermatitis; BOND\_PC; hypothetical protein MGC10820;  
KW hypothetical protein MGC10820 [Homo sapiens]; MGC10820;  
KW hypothetical protein LOC84734;  
KW hypothetical protein LOC84734 [Homo sapiens]; Clorf90;  
KW chromosome 1 open reading frame 90, isoform CRA\_b;  
KW chromosome 1 open reading frame 90, isoform CRA\_b [Homo sapiens];  
KW chromosome 1 open reading frame 90;  
KW chromosome 1 open reading frame 90 [Homo sapiens].

XX

OS Homo sapiens.

XX

PN WO200274961-A1.

XX

PD 26-SEP-2002.

XX

PF 14-MAR-2002; 2002WO-US005109.

Art Unit: 1647

XX  
PR 15-MAR-2001; 2001US-00810173.  
XX  
PA (HYSE-) HYSEQ INC.  
XX  
PI Tang YT, Zhou P, Goodrich R, Asundi V, Zhang J, Zhao QA, Ren F;  
PI Xue AJ, Yang Y, Ma Y, Yamazaki V, Chen R, Wang Z, Ghosh M;  
PI Wehrman T, Wang J, Wang D, Drmanac RT;  
XX  
DR WPI; 2003-040556/03.  
DR N-PSDB; ABX05372.  
DR PC:NCBI; gill10238585.  
DR PC:SWISSPROT; Q9BTA0.  
XX  
PT New isolated polypeptides and polynucleotides, useful for preventing,  
PT treating or ameliorating medical conditions, such as cancer,  
PT neurodegenerative disorders, lymphoid cell disorders, bone degenerative  
PT disorders, and infections.  
XX  
PS Claim 9; SEQ ID NO 913; 235pp; English.  
XX  
CC The invention relates to human polynucleotides and the polypeptides they  
CC encode. The polynucleotides and polypeptides are useful in diagnostics,  
CC forensics, gene mapping, medical imaging, identification of mutations  
CC responsible for genetic disorders or other traits, assessing biodiversity  
CC and producing many other types of data and products dependent on DNA and  
CC amino acid sequences. They are also useful for preventing, treating or  
CC ameliorating medical conditions, such as cancer, neurodegenerative  
CC disorders (e.g. Parkinson's disease, Alzheimer's disease), lymphoid cell  
CC disorders, osteoporosis, osteoarthritis, bone degenerative disorders,  
CC periodontal disease, liver fibrosis, infections (e.g. viral, fungal or  
CC bacterial) or autoimmune diseases (e.g. diabetes, atopic dermatitis).  
CC Sequences ABG99888-ABG99989 and ABU00010-ABU00433 represent human  
CC polypeptides of the invention. Note: The sequence data for this patent is  
CC not represented in the printed specification but is based on sequence  
CC information supplied by the European Patent Office  
CC  
CC Revised record issued on 15-JUN-2007 : Enhanced with precomputed  
CC information from BOND.  
XX  
SQ Sequence 163 AA;

Query Match 100.0%; Score 836; DB 1; Length 163;  
Best Local Similarity 100.0%;  
Matches 163; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MSLGLLKFFQAVGEEDEEDEEGESLDSVKALTAKLQLQTRRPSYLEWTAQVQSQAARRAQA 60  
|  
Db 1 MSLGLLKFFQAVGEEDEEDEEGESLDSVKALTAKLQLQTRRPSYLEWTAQVQSQAARRAQA 60  
  
Qy 61 KPGPGGPGDICGFDSMDSALEWLRRELREMQAQRQLAGQLRLRLRAQLHRLKMDQACHLH 120  
|  
Db 61 KPGPGGPGDICGFDSMDSALEWLRRELREMQAQRQLAGQLRLRLRAQLHRLKMDQACHLH 120  
  
Qy 121 QELLDEAELELELEPGAGLALAPLLRHLGLTRMNISARRFTLC 163  
|  
Db 121 QELLDEAELELELEPGAGLALAPLLRHLGLTRMNISARRFTLC 163

Upon further consideration, the Examiner found that Tang et al. does not anticipate the instant claims. The polypeptide corresponding to Tang et al. (SEQ ID NO: 913) is not associated with a polypeptide which can be employed for the treatment of liver or lung fibrosis. Tang et al. fail to teach any recognized animal models of fibrosis wherein SEQ ID NO:913 is administered. Further, the Tang reference would require one skilled in the art to pick and choose from various disclosures. The teachings of the Tang reference would not have indicated that the claimed polypeptide should have been used for the treatment of liver or lung fibrosis.

The Examiner provided Appel et al. as a reference of record (previous Office Action 8/12/09; page 5). This was in response to Applicant's arguments that Table 2 (of Tang et al.) indicates that the polypeptide of SEQ ID NO:913 has homology to the human SEC protein of the *sec* oncogene. Applicant cited page Table 2, page 177 of Tang et al. Applicant argued one skilled in the art, in view of the teachings of the reference, would have used the polypeptide associated with SEQ ID NO: 913 in methods of detecting cancers.

Appel et al. (European Journal of Human Genetics Vol. 10:17-25, 2002) teach keratolytic winter erythema (KWE) as an autosomal dominant skin disorder characterized by erythema, hyperkeratosis and peeling of the skin. The chromosomal region has been mapped to human chromosome 8p22-p23. Appel et al. teach to identify candidate genes for KWE, a BAC contig located between the markers at D8S550 and D8S1695 was constructed and sequenced. Twelve transcripts were identified between D8S550 and D8S1759. One transcript

Art Unit: 1647

(C8orf13) shows similarity to human SEC oncogene (abstract). Appel et al. teach C8orf13 with an open reading frame of 214 amino acid and shows similarities to the human SEC oncogene (37% in 83 residues)(page 22, last paragraph-1st paragraph, page 23). Appel et al. teach that in order to determine whether one of these transcripts was the KWE gene, exons belonging to a transcript was screened for mutations by sequencing genomic DNA from unaffected individuals and KWE patients (last paragraph, page 23). Appel et al. state that the KWE causing mutation was not identified in any of the transcripts, making it unlikely that one of these is the KWE gene (last paragraph, page 24).

The Examiner incorrectly stated that Appel et al. teach a possible correlation between human SEC protein. Appel et al. teach that as promoters and introns were not analyzed exhaustively, it cannot be excluded that one of the transcripts harbors the pathogenic mutation (last paragraph, page 24).

Listed below are Appendix B and Appendix C. Appendix B is an alignment between instant SEQ ID NOS: 2, 5, and 7 against the sequence referenced in Tang et al. for SEQ ID NO: 913. CAA365502 corresponds to GI36424 (i.e. human sec oncogene for SEC protein; see Table 2 of Tang et al.).

Appendix C (Results #s 1-3) is an alignment between instant SEQ ID NOS:2, 5 and 7 against CAC82740. CAC82740 is the amino acid sequence corresponding to C8orf13 of Appel et al. (see Table 1 of Appel et al., the nucleic acid sequence is Accession No. AJ301564). The final alignment in Appendix C (Result #4) is between CAC82740 (Appel et al.) and CAA36502 (the human sec oncogene sequence referenced by Tang in Table 2 on page 177).

Art Unit: 1647

The sequence alignments do not disclose a high percent identity between the instant SEQ ID NOs: and CAA365502 (GI36424 human sec oncogene for SEC protein; Tang et al.) or CAC82740 (C8orf13 of Appel et al.). The sequence alignments do not disclose a high percent identity between CAA365502 and CAC82740.

## **APPENDIX B**

GenCore version 6.3

Copyright (c) 1993 - 2011 Bioceleration Ltd.

OM protein - protein search, using sw model

Run on: May 4, 2011, 11:26:12 ; Search time 1 Seconds  
(without alignments)  
0.037 Million cell updates/sec

### **Title: US-10-570-122A-2**

Perfect score: 836

Sequence: 1 MSLGLLKFAQVGEEDEEDEE.....LLRHLGLTRMNISARRFTLC 163

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1 seqs, 109 residues

Total number of hits satisfying chosen parameters: 1

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : CAA36502.pep:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

#### SUMMARIES

Result No.	Score	% Match	Query Length	DB ID	Description
1	308	36.8	109	1 CAA36502	Sequence CAA36502

#### ALIGNMENTS

RESULT 1

CAA36502

; Sequence CAA36502, Application

## Art Unit: 1647

```
; GENERAL INFORMATION
; APPLICANT:
; APPLICANT:
; TITLE OF INVENTION:
; FILE REFERENCE:
; CURRENT APPLICATION NUMBER:
; CURRENT FILING DATE:
; PRIOR APPLICATION NUMBER:
; PRIOR FILING DATE:
; NUMBER OF SEQ ID NOS:
; SOFTWARE:
; SEQ ID NO CAA36502
; LENGTH:
; TYPE:
; ORGANISM:
CAA36502
```

```
Query Match          36.8%; Score 308; DB 1; Length 109;
Best Local Similarity 84.7%; Pred. No. 0;
Matches 61; Conservative 5; Mismatches 6; Indels 0; Gaps 0;
```

```
Qy          90 MQAQDRQLAGQLRLRLRAQLHRLKMDQACHLHQELLDEAELELELEPGAGLALAPLLRHLG 149
   |:||||||| :|||:||||:| | ||||| |||||:| | | | | |||
Db          1 MRAQDRQLAGQPVRLRLRLHRLKVDQVCHLHQELLDEAELEMELESGLPLAPPLRHLG 60

Qy          150 LTRMNISARRFT 161
   |||||
Db          61 LTRMNISARRFT 72
```

**Title: US-10-570-122A-5**

```
Perfect score: 445
Sequence: 1 MDSALEWLRLRELMQAQDR.....LLRHLGLTRMNISARRFTLC 88
```

```
Scoring table: BLOSUM62
               Gapop 10.0 , Gapext 0.5
```

```
Searched: 1 seqs, 109 residues
```

```
Total number of hits satisfying chosen parameters: 1
```

```
Minimum DB seq length: 0
Maximum DB seq length: 2000000000
```

```
Post-processing: Minimum Match 0%
                  Maximum Match 100%
                  Listing first 45 summaries
```

```
Database : CAA36502.pep:*
```

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	% Match	Query Length	DB ID	Description
1	308	69.2	109	1 CAA36502	Sequence CAA36502

## ALIGNMENTS

```
RESULT 1
CAA36502
; Sequence CAA36502, Application
```

```

; GENERAL INFORMATION
; APPLICANT:
; APPLICANT:
; TITLE OF INVENTION:
; FILE REFERENCE:
; CURRENT APPLICATION NUMBER:
; CURRENT FILING DATE:
; PRIOR APPLICATION NUMBER:
; PRIOR FILING DATE:
; NUMBER OF SEQ ID NOS:
; SOFTWARE:
; SEQ ID NO CAA36502
; LENGTH:
; TYPE:
; ORGANISM:
CAA36502

```

Query Match 69.2%; Score 308; DB 1; Length 109;  
Best Local Similarity 84.7%; Pred. No. 0;  
Matches 61; Conservative 5; Mismatches 6; Indels 0; Gaps 0;

```

Qy      15  MQAQDRQLAGQLRLRLRAQLHRLKMDQACHLHQELLDEAELELELEPGAGLALAPLLRHLG  74
      | : | | | | | | | | : | | | : | | | | : | | | | | | | | | | : | | | | | | | |
Db      1  MRAQDRQLAGQPVRLRLRLHRLKVDQVCHLHQELLDEAELEMELESGTGLPLAPPLRHLG  60

Qy      75  LTRMNISARRFT  86
      | | | | | | | |
Db      61  LTRMNISARRFT  72

```

**Title:** US-10-570-122A-7

Perfect score: 444  
Sequence: 1 IDSALEWLRRELREMOAQDR.....LLRHLGLTRMNISARRFTLC 88

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 1 seqs, 109 residues

Total number of hits satisfying chosen parameters: 1

```
Minimum DB seq length: 0
Maximum DB seq length: 2000000000
```

```
Post-processing: Minimum Match 0%
                  Maximum Match 100%
                  Listing first 45 summaries
```

Database : CAA36502.pep:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	308	69.4	109	1	CAA36502	Sequence CAA36502

## ALIGNMENTS

```
RESULT 1
CAA36502
; Sequence CAA36502, Application
```

Art Unit: 1647

```
; GENERAL INFORMATION
; APPLICANT:
; APPLICANT:
; TITLE OF INVENTION:
; FILE REFERENCE:
; CURRENT APPLICATION NUMBER:
; CURRENT FILING DATE:
; PRIOR APPLICATION NUMBER:
; PRIOR FILING DATE:
; NUMBER OF SEQ ID NOS:
; SOFTWARE:
; SEQ ID NO CAA36502
; LENGTH:
; TYPE:
; ORGANISM:
CAA36502
```

```
Query Match          69.4%; Score 308; DB 1; Length 109;
Best Local Similarity 84.7%; Pred. No. 0;
Matches 61; Conservative 5; Mismatches 6; Indels 0; Gaps 0;
```

```
Qy      15 MQAQDRQLAGQLRLRAQLHRLKMDQACHLHQELLDEAELELELEPGAGLALAPLLRHLG 74
      |:||||||| :|||:||||:| | ||||| |||||:| | | | | |||
Db      1  MRAQDRQLAGQPVRLRLRLHRLKVDQVCHLHQELLDEAELEMELESGLPLAPPLRHLG 60

Qy      75 LTRMNISARRFT 86
      |||||
Db      61 LTRMNISARRFT 72
```

```
Search completed: May 4, 2011, 11:26:12
Job time : 0.259587 secs
```

## **APPENDIX C**

GenCore version 6.3  
Copyright (c) 1993 - 2011 Bioceleration Ltd.

OM protein - protein search, using sw model

```
Run on:      May 4, 2011, 11:39:05 ; Search time 1 Seconds
              (without alignments)
              0.096 Million cell updates/sec
```

```
Title:      CAC82740
Perfect score: 1105
Sequence:    1 MSVPQIHVEEVGAEEGAGAA.....PLKLIGVTKMNINSRRFSLC 214
```

```
Scoring table: BLOSUM62
                Gapop 10.0 , Gapext 0.5
```

```
Searched:    4 seqs, 448 residues
```

```
Total number of hits satisfying chosen parameters:      4
```

```
Minimum DB seq length: 0
Maximum DB seq length: 2000000000
```

```
Post-processing: Minimum Match 0%
                  Maximum Match 100%
                  Listing first 45 summaries
```



## Art Unit: 1647

Database : seqs:\*  
 1: seqs/CAA36502.pep:\*  
 2: seqs/seqs.pep:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	325.5	29.5	163	2	US-10-570-122A-2	Sequence 2, Appli
2	216.5	19.6	88	2	US-10-570-122A-7	Sequence 7, Appli
3	213.5	19.3	88	2	US-10-570-122A-5	Sequence 5, Appli
4	156.5	14.2	109	1	CAA36502	Sequence CAA36502

## ALIGNMENTS

## RESULT 1

US-10-570-122A-2  
 ; Sequence 2, Application US/10570122A  
 ; GENERAL INFORMATION  
 ; APPLICANT: Power, Christine  
 ; APPLICANT:Lavrovsky, Yan  
 ; TITLE OF INVENTION: Treatment of Fibrotic Disease  
 ; FILE REFERENCE: ARS.122  
 ; CURRENT APPLICATION NUMBER: US/10/570,122A  
 ; CURRENT FILING DATE: 2006-02-28  
 ; PRIOR APPLICATION NUMBER: EP 03102723.8  
 ; PRIOR FILING DATE: 2003-09-08  
 ; NUMBER OF SEQ ID NOS: 20  
 ; SOFTWARE: PatentIn version 3.1  
 ; SEQ ID NO 2  
 ; LENGTH: 163  
 ; TYPE: PRT  
 ; ORGANISM: Homo sapiens  
 US-10-570-122A-2

Query Match 29.5%; Score 325.5; DB 2; Length 163;  
 Best Local Similarity 34.1%; Pred. No. 0;  
 Matches 73; Conservative 37; Mismatches 53; Indels 51; Gaps 3;

```

Qy      1 MSVPQIHVEEVGAEEGAGAAAPPDDHLRLSLKALTEKLRLETRRPSYLEWQARLEEHTWPF 60
        ||:  :  : || |:      : | |:|||| ||:|:||||||| |::: |
Db      1 MSLGLLKFFQAVGEDEEDEEG---ESLDSVKALTAKLQLQTRRPSYLEWTAQVQSQAW-- 55

Qy      61 PRPAAEPPQASLEEGGERGGQEPLPLREAGQHPPSARSASQGARPLSTGKLEGFQSIDEAI 120
        | |      | | : || |:| |:
Db      56 -----RRQAQKPGPGPGDTCGFDSDMSAL 80

Qy      121 AWLRKELTEMRLQDQQLARQLMRLRGDINKLKIEHTCR LHRRMLNDATYELEERDELADL 180
        |||:| | |: ||:| | |:| | |::|:|: | ||: |:|:| | |
Db      81 EWLRLRELMQAQDRQLAGQLRLRLRAQLHRLKMDQACHLHQELLDEAELELELEP----- 135

Qy      181 FCDSPASSFSLSTPLKLGVTMKNINSRRFSLC 214
        :  :|: | : |:|:|:|:|:|:|
Db      136 -----GAGLALAPLLRHLGLTRMNISARRFTLC 163

```

## RESULT 2

US-10-570-122A-7  
 ; Sequence 7, Application US/10570122A  
 ; GENERAL INFORMATION  
 ; APPLICANT: Power, Christine  
 ; APPLICANT:Lavrovsky, Yan

## Art Unit: 1647

; TITLE OF INVENTION: Treatment of Fibrotic Disease  
; FILE REFERENCE: ARS.122  
; CURRENT APPLICATION NUMBER: US/10/570,122A  
; CURRENT FILING DATE: 2006-02-28  
; PRIOR APPLICATION NUMBER: EP 03102723.8  
; PRIOR FILING DATE: 2003-09-08  
; NUMBER OF SEQ ID NOS: 20  
; SOFTWARE: PatentIn version 3.1  
; SEQ ID NO 7  
; LENGTH: 88  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-10-570-122A-7

Query Match 19.6%; Score 216.5; DB 2; Length 88;  
Best Local Similarity 42.4%; Pred. No. 0;  
Matches 42; Conservative 24; Mismatches 22; Indels 11; Gaps 1;

Qy 116 IDEAIAWLRKELTEMRLQDQQLARQLMRLRGDINKLKIEHTCRLHRRMLNDATYELEERD 175  
|| |: |||: || |: ||: ||| ||: ||| ::|||: | |: |:|: |||  
Db 1 IDSALEWLRRELREMQAQRQLAGQLLRRLRAQLHRLKMDQACHLHQELLDEAELELELEP 60  
  
Qy 176 ELADLFCDSPLASSFSLSTPLKLGVTMKNINSRRFSLC 214  
: :|: |: |:|: |||: |||: |||  
Db 61 -----GAGLALAPLLRHLGLTRMNISARRFTLC 88

## RESULT 3

US-10-570-122A-5  
; Sequence 5, Application US/10570122A  
; GENERAL INFORMATION  
; APPLICANT: Power, Christine  
; APPLICANT: Lavrovsky, Yan  
; TITLE OF INVENTION: Treatment of Fibrotic Disease  
; FILE REFERENCE: ARS.122  
; CURRENT APPLICATION NUMBER: US/10/570,122A  
; CURRENT FILING DATE: 2006-02-28  
; PRIOR APPLICATION NUMBER: EP 03102723.8  
; PRIOR FILING DATE: 2003-09-08  
; NUMBER OF SEQ ID NOS: 20  
; SOFTWARE: PatentIn version 3.1  
; SEQ ID NO 5  
; LENGTH: 88  
; TYPE: PRT  
; ORGANISM: Homo sapiens  
US-10-570-122A-5

Query Match 19.3%; Score 213.5; DB 2; Length 88;  
Best Local Similarity 41.4%; Pred. No. 0;  
Matches 41; Conservative 25; Mismatches 22; Indels 11; Gaps 1;

Qy 116 IDEAIAWLRKELTEMRLQDQQLARQLMRLRGDINKLKIEHTCRLHRRMLNDATYELEERD 175  
:| |: |||: || |: ||: ||| ||: ||| ::|||: | |: |:|: |||  
Db 1 MDSALEWLRRELREMQAQRQLAGQLLRRLRAQLHRLKMDQACHLHQELLDEAELELELEP 60  
  
Qy 176 ELADLFCDSPLASSFSLSTPLKLGVTMKNINSRRFSLC 214  
: :|: |: |:|: |||: |||: |||  
Db 61 -----GAGLALAPLLRHLGLTRMNISARRFTLC 88

## RESULT 4

CAA36502  
; Sequence CAA36502, Application  
; GENERAL INFORMATION  
; APPLICANT:  
; APPLICANT:  
; TITLE OF INVENTION:  
; FILE REFERENCE:  
; CURRENT APPLICATION NUMBER:

Art Unit: 1647

```
; CURRENT FILING DATE:
; PRIOR APPLICATION NUMBER:
; PRIOR FILING DATE:
; NUMBER OF SEQ ID NOS:
; SOFTWARE:
; SEQ ID NO CAA36502
; LENGTH:
; TYPE:
; ORGANISM:
CAA36502
```

```
Query Match          14.2%; Score 156.5; DB 1; Length 109;
Best Local Similarity 37.3%; Pred. No. 0;
Matches   31; Conservative   21; Mismatches   20; Indels   11; Gaps   1;
```

```
Qy      130 MRLQDQQLARQLMRLRGDINKLKIEHTCRLHRRMLNDATYELEERDELADLFCDSPASS 189
          || ||:|||| | :||| :::||:: | ||: |:|:| |:| :
Db      1  MRAQDRQLAGQPVRLRLRLHRLKVDQVCHLHQELLDEAELEMELES-----GTG 49

Qy      190 FSLSTPLKLIGVTKMNINSRRFS 212
          |: ||: |:|:| ||::| ||:
Db      50 LPLAPPLRHLGLTRMNISARRFT 72
```

```
Search completed: May 4, 2011, 11:39:05
Job time : 1 secs
```

### Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to REGINA M. DEBERRY whose telephone number is (571)272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1647

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARIANNE P ALLEN/  
Primary Examiner, Art Unit 1647

/R. M. D./  
Examiner, Art Unit 1647  
5/9/11